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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
SINGH, ANOOP KUMAR	
ART UNIT	PAPER NUMBER
1632	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/766,993	CHANG ET AL.	
	Examiner	Art Unit	
	ANOOP SINGH	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 May 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4,5,7-13 and 16-26* is/are pending in the application.

4a) Of the above claim(s) *16-17,22-24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4,5,7-13,18-21,25 and 26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment filed on May 13, 2009, has been received and entered. Claims 2-3, 6, 14-15, 27-66 have been canceled, while applicants have amended claims 1 and 4. Claims 1, 4-5, 7-13, 16-25 and 26 are pending.

Election/Restrictions

Applicant's election with traverse of the invention of claims 1-26 (group I) filed September 18, 2006 was acknowledged. It was noted that applicants elected 2D-CD4 as species for examination in a supplementary response filed on 12/ 28/2006. It is noted that claims 16-17, 22-24 do not read on elected species and therefore claims 16-17, 22-24 were also withdrawn. Claims 16-17, 22-24 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on September 18, 2006. The requirement was deemed proper and was therefore made FINAL.

Claims 1, 4-5, 7-13, 18-21, 25 and 26 are under examination.

Withdrawn -Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 4-5, 7-13, 15, 18-21, 25 and 26 were rejected under 35 U.S.C. 112, first paragraph. Applicants' amendments to the claims base claim is persuasive and instant specification enables one skilled in the art to make and/or use the invention directed to an isolated *Lactobacillus jensenii* bacterium comprising an expression cassette, the expression cassette comprising a promoter operably linked to polynucleotide encoding a signal sequence and a biologically-active polypeptide, wherein the biologically active polypeptide is expressed, is anchored to the cell wall of the *Lactobacillus* bacterium or is released from the *Lactobacillus*

bacterium, and is linked to a heterologous carboxyl terminal cell wall targeting region and wherein the cell wall targeting region comprises SEQ ID NO:7 or SEQ ID NO:8 or variants thereof in which LPQTG (SEQ ID NO:13) in SEQ ID NO:7 or SEQ ID NO:8 is replaced with LPQSG (SEQ ID NO:I 1), LPQAG (SEQ ID NO: 12), or LPQTA (SEQ ID NO: 14), and wherein the biologically active protein binds to a pathogen when the biologically active protein is contacted with the pathogen. It is noted that claims have been amended to include the limitations of expressed protein is expressed in the cell wall or is released from that is described in the instant specification (paragraph 65 and 67 of the specification) such that one of ordinary skill in the art would be able to practice the method as claimed without extensive or undue experimentation. Applicants' cite US Patent number 7,312,076 and argue that specification enables one of skill in the art to express any biologically active protein that binds to a pathogen when the biologically active protein is contacted with pathogen. These arguments have been fully considered and are persuasive commensurate with the scope of the elected specie.

Withdrawn- Double Patenting

Claims 1, 4-5, 7-13, 15, 18-21, 25 and 26 were provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-2 of copending Application No. 11/331,965 (now US patent 7,456011). Applicants' arguments pertaining to the issue of obviousness-type double patenting with claims in '965 is persuasive and therefore rejection is hereby withdrawn.

Maintained- Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting

ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 4-5, 7-13, 18-21, 25 and 26 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-12 of U.S. Patent No. US Patent 7,312,076 (application no 11/620,588). Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are directed to a *Lactobacillus jensenii* bacterium recombinantly altered to express any biologically active protein when it is contacted with a pathogen. Furthermore, '076(588) also discloses anchor sequences that are located at the carboxyl terminus of an encoded protein sequence that includes a cell wall associated sequence; the sequence LPQ(S/A/T)(G/A), where residues in parentheses indicate different options at that position; and a hydrophobic sequence, and, optionally, a charged sequence. The anchoring sequence comprises SEQ ID NO: 4 or 5 that has 100% sequence homology with SEQ ID NO 7 or 8 of the instant specification. It is noted that claims of '588 claims differ only with respect to a broader scope of biologically active protein and specific elements to recombinantly alter bacterium set forth in claims 1, 4-5, 7-13, 18-21, 25 and 26 that are broadly encompassed those specifically claimed in claims 1-12 of '076(588). Therefore, the claims 1, 4-5, 7-13, 18-21, 25 and 26 of the instant application are embraced by claims 1-12 of '076(588).

Response to the arguments

Applicants' arguments filed 5/13/09 have been fully considered but are not persuasive. Applicants ague that claims of the '076 patent are directed to a *Lactobacillusjensenii* bacterium recombinantly altered to express a biologically active protein, the present claim is directed to a non-obvious subset of L. *jensenii* that express a biologically active protein linked to a particular heterologous cell wall targeting sequence. Applicants argues that the cell wall targeting sequences in the present claims were not disclosed in other references, nor are they presented in the claims of the '076 patent. Applicants also assert that the priority application of

the '076 did not describe the specific anchoring sequences relied upon in the Office Action and thus the disclosure in the initial priority application.

In response, it is noted that base claim in the instant application is directed to an isolated *Lactobacillus jensenii* bacterium comprising an expression cassette, the expression cassette comprising a promoter operably linked to polynucleotide encoding a signal sequence and a biologically-active polypeptide, wherein the biologically active polypeptide is expressed, is anchored to the cell wall of the *Lactobacillus* bacterium or is released from the *Lactobacillus* bacterium, and is linked to a heterologous carboxyl terminal cell wall targeting region and wherein the cell wall targeting region comprises SEQ ID NO:7 or SEQ ID NO:8 and wherein the biologically active protein binds to a pathogen when the biologically active protein is contacted with the pathogen. In contrast, '076 (588) is directed to a *Lactobacillus jensenii* bacterium recombinantly altered to express a biologically active protein, wherein the biologically active protein binds to a pathogen when the biologically active protein is contacted with a pathogen. The dependent claims limit the *Lactobacillus jensenii*, wherein biologically active protein is secreted or displayed on the surface. It should be noted that '076 specifically teaches that in some embodiments the cell wall anchoring signal sequence comprises SEQ ID NO:4 or SEQ ID NO:5 that has 100% sequence homology with SEQ ID NO: 7 or 8 of the instant application (see figure 1B, C, col. 2, lines 30-55 and sequence search report). Furthermore, '076(588) also discloses anchor sequences that are located at the carboxyl terminus of an encoded protein sequence that includes a cell wall associated sequence; the sequence LPQ(S/A/T)(G/A), where residues in parentheses indicate different options at that position; and a hydrophobic sequence, and, optionally, a charged sequence. MPEP § 2111.01. states" those portions of the specification which provide support for the patent claims may also be examined and considered when addressing the issue of whether a claim in the application defines an obvious variation of an invention claimed in the patent. *In re Vogel*, 422 F.2d 438, 441-42, 164 USPQ 619, 622 (CCPA 1970). The court in Vogel recognized "that it is most difficult, if not meaningless, to try to say what is or is not an obvious variation of a claim," but that one can judge whether or not the invention claimed in an application is an obvious variation of an embodiment disclosed in the patent which provides support for the patent claim. With respect to applicants' argument of priority document, it is noted that instant rejection is made against the claims set forth in the

issued patent that embrace the anchoring sequences disclosed in the patent. Thus, contrary to applicants' assertion the breadth of base claim in '076, when taken in view of specific definition and specific embodiments described in the specification is clearly obvious over the base claim of the instant application. It is further noted that instant rejection was first made on 3/7/2007 and in response applicants have stated that the rejection be held in abeyance until the time of allowance of the application (see response filed on 8/6/2007).

New- Double Patenting

Instant rejection is necessitated by availability of application no 11/938,044 after the mailing of office action dated 2/19/09.

Claims 1, 4-5, 9, 11-13, 18-21, 25 and 26 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3, 5-6, 8-10 of copending Application No. 11/938044 in view of Boyd (US 6,193,982, IDS).

Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are directed to a *Lactobacillus jensenii* bacterium recombinantly altered to express any biologically active protein. In the instant case, base claim is directed to an isolated *Lactobacillus jensenii* bacterium comprising an expression cassette, the expression cassette comprising a promoter operably linked to polynucleotide encoding a signal sequence and a biologically-active polypeptide, wherein the biologically active polypeptide is expressed, is anchored to the cell wall of the *Lactobacillus* bacterium or is released from the *Lactobacillus* bacterium, and is linked to a heterologous carboxyl terminal cell wall targeting region and wherein the cell wall targeting region comprises SEQ ID NO:7 or SEQ ID NO:8 and wherein the biologically active protein binds to a pathogen when the biologically active protein is contacted with the pathogen. In contrast, '044 is directed to an isolated *Lactobacillus jensenii* bacteria recombinantly altered to express a protein. The dependent claims limit the *Lactobacillus jensenii*, wherein biologically active protein is secreted or displayed on the surface. It should be noted that claim 9 limits the *Lactobacillus jensenii* of claim 1, wherein the cell wall anchoring signal sequence comprises SEQ ID NO: 4 or 5 that has 100% sequence homology with SEQ ID NO: 7 and 8 of the instant application respectively (see claim 1-2, 4-5 and 9 sequence search report). In specific embodiments specification of '044 teaches that mucosal

surface-colonizing *Lactobacillus jensenii* bacteria recombinantly altered to express a biologically active protein (see para.9). Furthermore, it is disclosed that the expression cassettes can include promoter elements, sequences encoding signal sequences, a coding sequence for the polypeptide of interest and anchor sequences (para. 80, figure 1 B and 1C) polypeptides in Lactobacillus sp. can be any polypeptide including a receptor that viral or bacterial pathogens bind to infect a host (see para.88 and 91) meeting the limitation of claims 1, 4-5, 9, 11-13, 18-19, 25 and 26. With respect to the limitation of the expressing polypeptide is CD4 or an HIV-binding fragment of CD4, wherein CD4 or an HIV-binding fragment of CD4 bind to HIV, it is noted that Boyd teaches that cyanovirin-N, which binds to gp120 of immunodeficiency virus, can be used treat viral infections (columns 4, 6-7, and 15). Boyd teaches that exploiting the HIV gp120-targeting properties of sCD4 (also known as two-domain soluble CD4 protein) that was known to one of ordinary skill in the art (column 10). In addition, Boyd teaches that it is well established that lactobacilli can be readily transformed using available genetic engineering techniques (column 15). Boyd teaches that lactobacilli can be used as the delivery vehicle for a cyanovirin (columns 6-7 and 15-18). Boyd teaches that lactobacilli has been used against pathogenic bacterial or yeast infections of the urogenital tract based on the endogenous production of virucidal levels of H_2O_2 and/or lactic acid and/or other potentially virucidal substances (column 16). Boyd teaches that lactobacilli are prominent, nonpathogenic inhabitants of other body cavities (column 15). Thus, it would have been to combine the teaching to produce a genetically engineered *Lactobacillus jensenii* expressing a nucleotide sequence encoding a virus binding fragment to the vagina. One of ordinary skill in the art would have been motivated to combine the teaching to delivery a nucleotide sequence encoding 2D-CD4 using genetically engineered *Lactobacillus jensenii* to a mammalian's mucosal cells in vitro to study the binding of 2D-CD4 to a viral pathogen as taught by Boyd (columns 15-17 and 39). In view of the teaching of, one of ordinary skill in the art would have a reasonable expectation of success for producing the claimed *Lactobacillus jensenii*. Thus, the instant claims are obvious variants of the claims in co pending application '044 when viewed in light of the teachings of Boyd.

This is a provisional obviousness-type double patenting rejection.

Conclusion

No claims allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ANOOP SINGH whose telephone number is (571)272-3306. The examiner can normally be reached on 9:00AM-5:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on (571) 272- 4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Deborah Crouch/
Primary Examiner, Art Unit 1632

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